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**Allergy immunotherapy in ABPA**

11/14/2006

**Q.**

I am treating a young college student with severe asthma. She was sent to me by a scholarly pulmonologist for help in controlling her asthma from my atopic point of view. She was recently diagnosed with ABPA. She is on maximal medications with good compliance but poor control. Her IgE is too high for Xolair use. She had immunotherapy as a child and reports having a good response.

I was taught to not give IT in ABPA during fellowship.

Is there any role for such for allergens other than *Aspergillus fumigatus* in such a case?

**A.**

I had my own thought as to how to respond to your question. However, I wanted to see what an expert in ABPA said about this matter. Therefore, I obtained input from Dr. Raymond Slavin of the St. Louis Univ. School of Medicine, an expert in ABPA. His thoughtful response is enclosed below.

**Dr. Slavin's comments:**

As usual, you express great insights. IT with antigens other than aspergillus can certainly be given in ABPA. They generally have many sensitivities other than to aspergillus. The only objection to using aspergillus is the theoretical one of giving an antigen to which the patient has a precipitating antibody with the possibility of creating an immune complex disease. This was predicated years ago by Jack Pepys and despite no evidence of this ever happening, people have shied away from including aspergillus in the treatment mix.

As an aside, the ABPA committee of the AAAAI has proposed a study to Genentech using Xolair in the treatment of ABPA. Lots of good reasons to consider it since Xolair does so much more than simply reducing IgE levels i.e., decreasing Fc receptors and affecting antigen recognition in antigen presenting cells.

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**Bronchopulmonary Aspergillosis with a Negative Skin Test to Aspergillus**

5/24/2008

**Q.**

I am a new allergist in private practice. I was recently referred a patient by a pulmonologist who was diagnosed with ABPA. The pulmonologist had already done all of the lab testing including total IgE, aspergillus specific IgE and IgG and precipitating antibody - all of which were positive. The patient was sent to me for skin testing to aspergillus. Unfortunately, he was on high doses of prednisone and fexofenadine. We tested him to aspergillus with a positive and negative control, which were all negative.

**My question is this:**

Is there anything else I can do other than have him come back when he is able to decrease his prednisone and off of the antihistamine? Also, what does the skin test tell us that the specific IgE does not?

**A.**

The explanations for your negative skin tests could be as follows:

1. Did you do only an epicutaneous test, or an intradermal? Intradermals are often required, and if you did not do one, I would repeat the test using an intradermal.
2. Of course, the fexofenadine could be suppressing the test.
3. Alternatively, I will quote you from Dr. Paul Greenberger's chapter in Allergy: Principles and Practice (1): "The quality of aspergillus extracts used for skin testing or serologic assays may be poor in that few relevant aspergillus epitopes will be present. True negative but inaccurate skin testing or serologic results will occur and are misleading. Some aspergillus mixes available commercially do not contain aspergillus fumigatus, so physicians may need to purchase specific reactive extracts for skin testing."

On the basis of the other findings, I feel that your patient does have allergic bronchopulmonary aspergillosis, and your skin test is negative for one of the above reasons.

It might be helpful, if a high resolution CT scan of the chest has not been done, to pursue this study. If the patient has central bronchiectasis, you will certainly be able to confirm the diagnosis.

Finally, if your ELISA tests were done commercially, and you wish a more definitive confirmation, you could send serum to Dr. Greenberger's laboratory. His contact information is noted below:

I should tell you ahead of time that this laboratory does charge fees for these tests, and you will need to make arrangements with the patient or the insurance company to make sure that financial coverage will be offered.

Normally, prednisone would not depress the skin test reactivity to any great extent, but of course fexofenadine can. Therefore I clearly would bring the patient back and redo the skin tests, making sure that your extract is well standardized and does contain

aspergillus fumigatus by contacting the supplier. I would also suggest employing extract from at least two different suppliers and applying an intradermal test if the epicutaneous test was negative

And in answer to your last question - about the skin test versus the in vitro test: In most instances, the skin test, as you know, is more sensitive, and it has been the classical approach to establishing a patient at risk for allergic bronchopulmonary aspergillosis. However, both tests offer the same basic information.

Thank you again for your inquiry, and I hope this information has been helpful to you.

**Reference:**

1. Greenberger P. Allergic bronchopulmonary aspergillosis. In: Allergy: Principles and Practice, 6th Edition, edited by Middleton, Adkinson, Yunginger, Busse, Bachner, Holgate, and Simons (Mosby-Year Book, Inc., St. Louis, Missouri), Volume II, page 1353, 2003.

Sincerely,  
Phil Lieberman, MD

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**Immunotherapy in a patient with allergic bronchopulmonary aspergillosis**

8/6/2009

**Q. Would immunotherapy potentially worsen a patient with allergic bronchopulmonary aspergillus if aspergillus is in the vaccine? If so, would IT to other relevant aeroallergens be beneficial? (leaving Aspergillus out of vaccine)**

**A.** Thank you for your recent inquiry.

There is no direct evidence that immunotherapy using aspergillus antigen would be harmful to a patient with allergic bronchopulmonary aspergillosis. The admonition against immunotherapy in such a patient is that it may produce IgG anti-aspergillus antibodies, and this class of antibodies has been postulated to play a role in the pathogenesis of the disease. However, there has been no documentation either in case reports or studies designed to assess this hypothesis. Certainly there would be no problem administering immunotherapy to other relevant aeroallergens.

Perhaps the best way to summarize this issue for you is to quote Dr. Paul Greenberger's comments in his chapter in Patterson's Allergic Diseases (1).

"Immunotherapy with aspergillus species probably should not be administered in patients with ABPA, but examples of adverse effects aside from injection reactions have not been reported. It is not expected that immunotherapy with aspergillus extracts would result in immune complex formation. Immunotherapy can be administered with pollens and mites and possibly fungi, but not those in the aspergillus genus."

Thank you again for your inquiry and we hope this response is helpful to you.

**Reference:**

1. Greenberger P. In: Patterson's Allergic Diseases, Lippincott and Williams, 6th edition, 2002, Page 351.

Sincerely,

Phil Lieberman, M.D.

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**Serologic testing in ABPA**

9/23/2004

**Q.** In working up a patient for ABPA, I've read that serological diagnostic tests include:

**Precipitins to Aspergillus**

**Specific IgE to Aspergillus**

**Specific IgG to Aspergillus**

However, I thought that the Precipitins are IgG.

**Questions:**

**1) What's the difference between precipitins to Aspergillus and specific IgG to aspergillus?**

**2) Are both precipitins and specific IgG to aspergillus needed?**

**3) Do most major commercial labs do both these tests?**

**A.** To respond to your questions with the latest information available, I obtained input from Dr. Paul Greenberger of the Northwestern Univ. Medical Center, one of the leading investigators of ABPA in the world. His response is enclosed below. My overall impression is that finding high levels of anti-A. fumigatus IgE antibodies by an ELISA done in a reliable lab is the best current way of distinguishing ABPA from just asthma when the patient exhibits a positive skin test to A. Fumigatus.

Dr. Greenberger's comments:

1. Precipitins in gel represent IgG antibodies that are present in high concentration (can be detected for certain antibodies in patients with SLE and MCTD). For the Aspergillus testing, sera are concentrated before testing by precipitin assay. For the anti-Aspergillus ELISA tests, sera are diluted to 1:1000 and 1:5000 so that the optical density of the assay can be useful to compare the test sera with control or sera from patients with asthma without ABPA. Both tests measure anti-Aspergillus antibodies but by diluting the sera, it is possible to have a discriminatory test to distinguish ABPA from aspergillus-skin test positive asthma, both of whom have loads of anti Aspergillus IgE and IgG.

2. Because up to 10% of patients with asthma may have serum precipitins to A fumigatus, they are not specific regarding ABPA. Properly performed positive anti-Aspergillus ELISA or unicaps could eliminate the need for precipitin testing. Nevertheless, because we don't have accepted recombinant allergens (22 for Af) that are approved for ELISA testing and because some labs use poorly reactive extracts, precipitins may still have a place.

3. Quest sends the ABPA bloods to us from several med centers. I am not sure what some commercial labs are doing.

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